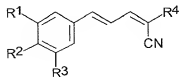


We claim:

1. A compound of Formula I, and salts, solvates or hydrates thereof:



I

wherein

R^1 and R^2 are each independently selected from the group consisting of H, OH, C_{1-6} alkyl, C_{1-6} alkoxy, NH_2 , $NH-C_{1-6}$ alkyl, $N(C_{1-6}alkyl)(C_{1-6}alkyl)$, SH, $S-C_{1-6}alkyl$, $O-Si(C_{1-6}alkyl)(C_{1-6}alkyl)(C_{1-6}alkyl)$, NO_2 , CF_3 , OCF_3 and halo;

R^3 is selected from the group consisting of H, OH, C_{1-6} alkyl, C_{1-6} alkoxy, NH_2 , $NH-C_{1-6}$ alkyl, $N(C_{1-6}alkyl)(C_{1-6}alkyl)$, SH, $S-C_{1-6}alkyl$, $O-Si(C_{1-6}alkyl)(C_{1-6}alkyl)(C_{1-6}alkyl)$, NO_2 , halo and $CH_2-S-(CH_2)_n$ Ar;

R^4 is selected from the group consisting of $C(X)R^5$, SO_3Ar , NH_2 , $NH-C_{1-6}alkyl$, $N(C_{1-6}alkyl)(C_{1-6}alkyl)$, $P(O)(OH)_2$, $P(O)(OC_{1-6}alkyl)_2$, and $C(NH_2)=C(CN)_2$;

X is selected from O, S, NH and $N-C_{1-6}alkyl$;

R^5 is selected from the group consisting of NH_2 , OH, $NH(CH_2)_p$ Ar, $NH(CH_2)_pOH$, $(CH_2)_pOC_{1-6}alkyl$, $C_{1-6}alkyl$, $C_{1-6}alkoxy$, $NHNH_2$, $NHC(O)NH_2$, $NHC(O)C_{1-6}alkoxy$, N-morpholino and N-pyrrolidino; and

Ar is an aromatic or heteroaromatic group, unsubstituted or substituted with 1-4 substituents, independently selected from the group consisting of OH, $C_{1-6}alkyl$, $C_{1-6}alkoxy$, NH_2 , $NH-C_{1-6}alkyl$, $N(C_{1-6}alkyl)(C_{1-6}alkyl)$, SH, $S-C_{1-6}alkyl$, NO_2 , CF_3 , OCF_3 and halo;

n is 0 to 4; and

p is 1-4.

2. The compound according to claim 1, wherein R^1 and R^2 are each independently selected from the group consisting of H, OH, $C_{1-4}alkyl$, C_{1-4}

alkoxy, NH₂, NH-C₁₋₄alkyl, SH, S-C₁₋₄alkyl, O-Si(C₁₋₄alkyl)(C₁₋₄alkyl)(C₁₋₄alkyl), NO₂, CF₃, OCF₃ and halo.

3. The compound according to claim 2, wherein R¹ and R² are each independently selected from the group consisting of H, OH, OCH₃, O-Si(CH₃)₂(^tBu), S-Me, SH and NO₂.

4. The compound according to claim 3, wherein R¹ and R² are both OH or R¹ and R² are both OCH₃.

5. The compound according to claim 4, wherein R¹ is OCH₃ and R² is OH.

6. The compound according to claim 1, wherein R³ is selected from the group consisting of H, OH, C₁₋₄alkyl, C₁₋₄alkoxy, NH₂, NH-C₁₋₄alkyl, N(C₁₋₄alkyl)(C₁₋₄alkyl), SH, S-C₁₋₄alkyl, NO₂ and halo.

7. The compound according to claim 6, wherein R³ is selected from the group consisting of H, OH, OCH₃, SH, SMe, NO₂ and halo.

8. The compound according to claim 7, wherein R³ is selected from the group consisting of H, OH and OCH₃.

9. The compound according to claim 1, wherein R⁴ is selected from the group consisting of C(X)R⁵ and C(NH₂)=C(CN)₂.

10. The compound according to claim 9, wherein R⁴ is C(X)R⁵.

11. The compound according to claim 10, wherein X is selected from the group consisting of O and S.

12. The compound according to claim 10, wherein R⁵ is selected from the group consisting of NH₂, OH, NH(CH₂)_pAr, NH(CH₂)_pOH and C₁₋₄alkoxy.

13. The compound according to claim 12, wherein p is 1-3.

14. The compound according to claim 13, wherein R^5 is selected from the group consisting of NH_2 , OH, $NH(CH_2)_pAr$, $NH(CH_2)_pOH$ and OCH_3 .

15. The compound according to claim 14, wherein p is 1-2.

16. The compound according to claim 1, wherein Ar is an unsubstituted phenyl group or a phenyl group substituted with 1-4 substituents optionally selected from the group consisting of OH, $C_{1-6}alkyl$, $C_{1-6}alkoxy$, NH_2 , $NH-C_{1-6}alkyl$, $N(C_{1-6}alkyl)(C_{1-6}alkyl)$, SH, $S-C_{1-6}alkyl$, NO_2 , CF_3 , OCF_3 and halo.

17. The compound according to claim 14, wherein Ar is an unsubstituted phenyl group or a phenyl group substituted with 1-4 substituents optionally selected from the group consisting of OH, $C_{1-6}alkyl$, $C_{1-6}alkoxy$, NH_2 , $NH-C_{1-6}alkyl$, $N(C_{1-6}alkyl)(C_{1-6}alkyl)$, SH, $S-C_{1-6}alkyl$, NO_2 , CF_3 , OCF_3 and halo.

18. The compound according to any of claims 16 or 17, wherein Ar is an unsubstituted phenyl group or phenyl group substituted with 1-2 substituents optionally selected from the group consisting of OH, $C_{1-4}alkyl$, $C_{1-4}alkoxy$, NH_2 , $NH-C_{1-4}alkyl$, $N(C_{1-4}alkyl)(C_{1-4}alkyl)$, SH, $S-C_{1-4}alkyl$, NO_2 , CF_3 , OCF_3 and halo.

19. The compound according to claim 18, wherein Ar is an unsubstituted phenyl group or phenyl group substituted with 1-2 substituents optionally selected from the group consisting of OH, OCH_3 , NH_2 , $NHCH_3$, $N(CH_3)_2$, SH, SCH_3 , CF_3 , OCF_3 and halo.

20. The compound according to claim 19, wherein Ar is selected from the group consisting of phenyl and 3,4-dihydroxyphenyl.

21. The compound according to claim 1, selected from the group consisting of:

(*E,E*)-2-(benzylamido)-3-styrylacrylonitrile (CR1);

(*E,E*)-2-(benzylamido)-3-(3,4-dimethoxystyryl)acrylonitrile (CR2);

5 (*E,E*)-2-(benzylamido)-3-(3,5-dimethoxy-4-hydroxystyryl)acrylonitrile (CR3);

(*E,E*)-2-(benzylamido)-3-(3,4-dihydroxystyryl)acrylonitrile (CR4);

(*E,E*)-2-(phenylethylamido)-3-(3,4-dimethoxystyryl)acrylonitrile (CR5);

10 (*E,E*)-2-(phenylethylamido)-3-(3,5-dimethoxy-4-hydroxystyryl)acrylonitrile (CR8);

(*E,E*)-2-(phenylpropylamido)-3-(3,5-dimethoxy-4-hydroxystyryl)acrylonitrile (CR9);

(*E,E*)-2-(3,4-dihydroxybenzylamido)-3-(3,5-dimethoxy-4-hydroxystyryl)acrylonitrile (CR11);

15 (*E,E*)-2-thioacetamido-3-(3,5-dimethoxy-4-hydroxystyryl)acrylonitrile (CR12);

(*E,E*)-2-acetamido-3-(3,5-dimethoxy-4-hydroxystyryl)acrylonitrile (CR13);

(*E,E*)-2-carboxy-3-(3,5-dimethoxy-4-hydroxystyryl)acrylonitrile (CR14);

20 (*E,E*)-2-carbomethoxy-3-(3,5-dimethoxy-4-hydroxystyryl)acrylonitrile (CR15);

(*E,E*)-2-acetamido-3-[3,4-bis(*t*-butyldimethylsilyloxystyryl)]acrylonitrile (CR16);

(*E,E*)-2-acetamido-3-(3,4-dihydroxystyryl)acrylonitrile (CR17);

25 (*E,E*)-2-(benzylamido)-3-(3,4-bis(*t*-butyldimethylsilyloxystyryl))acrylonitrile (CR18);

(*E,E*)-2-(3,4 dihydroxybenzylamido)-3-styrylacrylonitrile (CR19);

(*E,E*)-2-(3,4 dihydroxybenzylamido)-3-[3,4-bis(*t*-butyldimethylsilyloxystyryl)]acrylonitrile (CR20);

30 (*E,E*)-2-(3,4 dihydroxybenzylamido)-3-(3,4-dihydroxystyryl)acrylonitrile (CR21);

(*E,E*)-2-(β -ethanolamido)-3-(3,5-dimethoxy-4-hydroxystyryl)acrylonitrile (CR24);

(*E,E*)-2-(benzylamido)-3-(4-nitrostyryl)acrylonitrile (CR27);

(*E,E*)-2-(3,4-dihydroxybenzylamido)-3-(4-nitrostyryl)acrylonitrile (CR28);

and

(*E,E*)-2-(1-amino-2,2-dicyanoethenyl)-3-(4-nitrostyryl)acrylonitrile

(CR29).

22. The compound according to claim 21, selected from the group consisting of:

(*E,E*)-2-(benzylamido)-3-styrylacrylonitrile (CR1);

(*E,E*)-2-(benzylamido)-3-(3,4-dimethoxystyryl)acrylonitrile (CR2);

(*E,E*)-2-(benzylamido)-3-(3,5-dimethoxy-4-hydroxystyryl)acrylonitrile (CR3);

(*E,E*)-2-(benzylamido)-3-(3,4-dihydroxystyryl)acrylonitrile (CR4);

(*E,E*)-2-(phenylethylamido)-3-(3,4-dimethoxystyryl)acrylonitrile (CR5);

(*E,E*)-2-(phenylpropylamido)-3-(3,5-dimethoxy-4-hydroxystyryl)acrylonitrile (CR9);

(*E,E*)-2-(3,4-dihydroxybenzylamido)-3-(3,5-dimethoxy-4-hydroxystyryl)acrylonitrile (CR11);

(*E,E*)-2-thioacetamido-3-(3,5-dimethoxy-4-hydroxystyryl)acrylonitrile (CR12);

(*E,E*)-2-acetamido-3-(3,5-dimethoxy-4-hydroxystyryl)acrylonitrile (CR13);

(*E,E*)-2-carboxy-3-(3,5-dimethoxy-4-hydroxystyryl)acrylonitrile (CR14);

(*E,E*)-2-carbomethoxy-3-(3,5-dimethoxy-4-hydroxystyryl)acrylonitrile (CR15);

(*E,E*)-2-acetamido-3-(3,4-dihydroxystyryl)acrylonitrile (CR17);

(*E,E*)-2-(3,4-dihydroxybenzylamido)-3-styrylacrylonitrile (CR19);

(*E,E*)-2-(3,4-dihydroxybenzylamido)-3-(3,4-dihydroxystyryl)acrylonitrile (CR21); and

(*E,E*)-2-(β -ethanolamido)-3-(3,5-dimethoxy-4-hydroxystyryl)acrylonitrile (CR24).

23. The compound according to claim 22, selected from the group consisting of:

(*E,E*)-2-(benzylamido)-3-(3,4-dihydroxystyryl)acrylonitrile (CR4);

(*E,E*)-2-(3,4-dihydroxybenzylamido)-3-(3,5-dimethoxy-4-hydroxystyryl)acrylonitrile (CR11);

(*E,E*)-2-acetamido-3-(3,4-dihydroxystyryl)acrylonitrile (CR17);

(*E,E*)-2-(3,4-dihydroxybenzylamido)-3-styrylacrylonitrile (CR19);

(*E,E*)-2-(3,4-dihydroxybenzylamido)-3-(3,4-dihydroxystyryl)acrylonitrile (CR21); and

(*E,E*)-2-(β -ethanolamido)-3-(3,5-dimethoxy-4-hydroxystyryl)acrylonitrile (CR24).

24. The compound (*E,E*)-2-(benzylamido)-3-(3,4-dihydroxystyryl)acrylonitrile (CR4).

25. The compound (*E,E*)-2-(3,4-dihydroxybenzylamido)-3-(3,5-dimethoxy-4-hydroxystyryl)acrylonitrile (CR11).

26. The compound (*E,E*)-2-(3,4-dihydroxybenzylamido)-3-(3,5-dimethoxy-4-hydroxystyryl)acrylonitrile (CR11).

27. A composition comprising a compound according to claim 1 in admixture with a pharmaceutically acceptable diluent or carrier.

28. A method of modulating cell proliferation comprising administering an effective amount of a compound of claim 23 to modulate cell proliferation to a cell or animal in need thereof.

29. A method of inhibiting cell proliferation comprising administering an effective amount of a compound of claim 23 to inhibit cell proliferation to a cell or animal in need thereof.

5 30. The method of claim 29, wherein the cell proliferation that is inhibited is cancer cell proliferation.

31. A method of treating cancer comprising administering to an animal in need thereof an effective amount of a compound of claim 23.

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32. The method of claim 30 or 31 wherein said cancer is a hematopoietic cell cancer.

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33. The method of claim 30 or 31 wherein said cancer is a leukemia, a lymphoma, a myeloma or a carcinoma.

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34. The method of claim 33 wherein said leukemia is acute lymphoblastic leukemia, aggressive Philadelphia+ leukemia, acute myelocytic leukemia, chronic myeloid leukemia, chronic lymphocytic leukemia or juvenile myelomonocyte leukemia.

35. The method of claim 34 wherein said leukemia is acute lymphoblastic leukemia.

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36. A method of modulating cell proliferation comprising administering an effective amount of a compound capable of modulating cell proliferation according to claim 1 or a composition of claim 27 to a cell or animal in need thereof.

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37. A method of inhibiting cell proliferation comprising administering an effective amount of a compound capable of inhibiting cell proliferation

according to claim 1 or a composition according to claim 27 to a cell or animal in need thereof.

38. A method of inhibiting cancer cell proliferation comprising administering
5 an effective amount of a compound capable of inhibiting cancer cell proliferation according to any one of claim 1 or a composition according to claim 27 to a cell or animal in need thereof.

39. A method of treating cancer comprising administering an effective
10 amount of a compound capable of inhibiting cancer cell proliferation according to claim 1 or a composition according to claim 27 to a cell or animal in need thereof.

40. A method according to claim 38 or 39 wherein said cancer is a
15 hematopoietic cell cancer.

41. A method according to claim 38 or 39 wherein said cancer is a
leukemia, a lymphoma, a myeloma or a carcinoma.

41. A method according to claim 41 wherein said leukemia is acute
20 lymphoblastic leukemia, aggressive Philadelphia+ leukemia, acute myelocytic leukemia, chronic myeloid leukemia, chronic lymphocytic leukemia or juvenile myelomonocyte leukemia,

43. A method according to claim 42 wherein said leukemia is acute
25 lymphoblastic leukemia.